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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/756,095 | 01/08/2001 | Lloyd G. Mitchell | A31304-B-A-A<br>072874.0134 | 5645 |

21003 7590 05/20/2003

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| EXAMINER | |
|---|---|
| SULLIVAN, DANIEL M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 05/20/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/756,095 | MITCHELL ET AL. | |
| | Examiner | Art Unit | |
| | Daniel M Sullivan | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 January 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

This is the First Office Action on the Merits of the application filed 8 January 2001, which is a CIP of 09/158,863 filed 09/23/1998 (now U.S. Patent No. 6,280,978), which is a CIP of 09/133,717 filed 08/13/1998 (now U.S. Patent No. 6,083,702), which is a CIP of 09/087,233 filed 05/28/1998 (now abandoned), which is a CIP of 08/766,354 filed 12/13/1996 (now U.S. Patent No. 6,013,487), which claims benefit of U.S. provisional application 60/008,717 filed 12/15/1995. Claims 1-43 are pending in the application.

The substitute specification filed 4 October 2001 has been entered.

### *Election/Restrictions*

In the response filed 24 March 2003 (Paper No. 11) Applicant argues persuasively for withdrawal of the restriction requirement set forth in the Office Action mailed 30 September 2002 (Paper No. 9). Therefore, claims 1-43 are examined herein.

### *Priority*

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Specifically, there is no support for a target binding domain limited to between 10 and 600 nucleotides in length in the parent applications. Therefore, claims 1-24 will be afforded a priority date of 8 January 2001.

### *Oath/Declaration*

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Specifically, the serial number of the provisional application on page 2 has been altered.

### *Drawings*

The drawings are objected to for the reasons indicated on the attached PTO-948. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

### INFORMATION ON HOW TO EFFECT DRAWING CHANGES

**1. Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and

application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

**Timing of Corrections**

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

***Claim Objections***

Claim 26 objected to because of the following informalities: The claim contains editor's markings. Applicant should provide a clean copy of the claim. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is indefinite in the recitation of "the translatable protein product". There is no antecedent basis for the phrase in claims 16 or 17, from which claim 20 depends. Amending the claim such that it depends from claim 19 would be remedial.

Claim 26 is indefinite in the recitation of "the target binding domain". There is no antecedent basis for the limitation in the claim. Claim 26 is additionally indefinite in being directed to a process which omits a step (i.e., step b)). In the interest of compact prosecution, the claim has been examined with the assumption that the claim should be formatted like claim 25. That is, step c) should be deleted and step d) should be labeled step b). Amending the claim accordingly would obviate this rejection.

Claim 28 is indefinite insofar as it depends from claim 26.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-27, 29-34, 36 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 9-16, 18-21 23, 25 and 32-34 of U.S. Patent No. 6,013,487 (hereinafter '487). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant claims 1, 2, 3, 4, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 and 23 recite the same limitations as claims 1, 9, 2, 3, 5, 10, 12, 11, 13, 18, 14, 15, 16, 19, 20, 21, 23, 25, 32, 34 and 33 of '487, respectively, except that the instant claims are further limited to a target binding domain that is between 10 and 600 nucleotides in length. In column 4, '487 teaches that the binding domains should be at least 15-30 nucleotides in length and up to several hundred nucleotides. In column 3, '487 teaches, "[l]onger complementary sequences increase the stability of the duplex, but very long regions can interact with multiple mRNAs through base paring involving only 510 contiguous bases, thus lowering their specificity". Thus, '487 clearly teaches that it is desirable that the binding domain be greater than 15-30 nucleotides in length but not greater than several hundred nucleotides. Therefore, a binding domain having a length which falls within the range of 10-600 nucleotides, and thus the instant invention as a whole, would have been obvious to the ordinary skilled artisan in possession of U.S. Patent No. 6,013,487.

Claims 5 and 24 limit the nucleic acid molecule of the claims from which they depend to comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the splice region. The claims as a whole would be obvious to one of ordinary skill in the art in view of the limitations of '487 claims 9, 21 or 22 and the teachings in column 4 of '487 which provide that incorporation of a "safety", which covers elements of the 3' and/or 5' splice site, prevents undesirable non-specific trans-splicing.

Claim 7 limits the nucleic acid molecules of the claims from which it depends to comprising a translational stop codon. The claim as a whole would be obvious to one of ordinary skill in the art in view of the limitations '487 claims 1 or 2 and the teaching in column 6, lines 49-51, that the incorporation of stop codons in the spacer region would block translation of an unspliced pre-therapeutic RNA.

The instant claims 25, 26, 27, 29, 30, 31, 32, 33, 34, 36 and 37 omit process steps set forth in '487 claims 1, 9, 2, 10, 12, 11, 13, 18, 14, 32 and 34, respectively, which merely broadens the scope of the patented claims in a nonspecific manner. Thus, the claims of '487 fall entirely within the scope of the instant claims or, in other words, the instant claims are anticipated by the claims of '487. Therefore, the instant claimed subject matter is obvious in view of the patented claims.

Claims 25-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 7-13, 15, 25-30, 32 and 33 of U.S. Patent No. 6,083,702 (hereinafter '702). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims differ from the patented claims only in the omission of specific process steps. Claims 1, 2, 3, 7, 8, 9, 10, 11, 12, 13, 15, 25, 26, 27, 28, 29, 30, 32 and 33 fall entirely within the scope of the instant claims 25-33, respectively. Therefore, the instant claims are anticipated by the patented claims and would be obvious in view thereof.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6, 8, 11, 14-16, 19-21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Puttaraju *et al.* (1999) *Nat. Biotechnol.* 17:246-252.

Independent claim 1 is directed to a cell comprising a nucleic acid molecule wherein the nucleic acid molecule comprises: a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length; b) a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site; c) a spacer region that separates the 3' splice region from the target binding domain; and d) nucleotide sequence to be trans-spliced, wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell. Independent claim 8 is directed to a cell comprising a vector wherein the vector expresses a nucleic acid molecule having the limitations of the nucleic acid molecule of claim 1. Independent claim 11 is directed to a method of producing a chimeric RNA molecule in a cell comprising contacting a target pre-mRNA in the cell with a nucleic acid molecule comprising the limitations of the nucleic acid molecule of claim 1. Independent claim 16 is directed to a nucleic acid molecule comprising each of the limitations of the nucleic acid molecule of clam 1 and further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site. Independent claim 21 is directed to an expression vector which express a nucleic acid molecule comprising the limitations of the nucleic acid molecule of claim 1.

Puttaraju *et al.* teaches a nucleic acid molecule comprising a target binding domain 18 nucleotides in length, a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site, a spacer region that separates the 3' splice region from the target binding domain, and a nucleotide sequence to be trans-spliced (see especially Figure 1 and the caption thereto, and Table 1). In figure 2 and the caption thereto, Puttaraju *et al.* teaches that the specificity of trans-splicing is improved by the inclusion of a safety sequence according to independent claim 16 and dependent claims 4 and 24. The nucleic acid molecule of Puttaraju *et al.* thus comprises all of the limitations of the nucleic acid molecules of the independent claims. In the second column on page 249, Puttaraju *et al.* teaches a cell comprising a vector which expresses the nucleic acid molecule, and in the section bridging pages 249 and 250, Puttaraju *et al.* teaches a method of producing a chimeric RNA molecule in a cell comprising contacting a target pre-mRNA in the cell with a nucleic acid molecule. Therefore, the teachings of Puttaraju *et al.* anticipate all of the limitations of the instant independent claims and dependent claim 4 and 24. Puttaraju *et al.* further teaches the nucleic acid molecule which further comprises sequences encoding a translatable protein product (i.e., lacZ) according to the limitations of claims 6, 14 and 19 (see especially the paragraph bridging pages 249 and 250 and Figure 6 and the caption thereto), and comprising a sequence encoding a toxin according to the limitations of claims 15 and 20 (see especially Figure 1 and the caption thereto). As Puttaraju *et al.* teaches each of the limitations of the claimed invention, the claims are anticipated by Puttaraju *et al.*

Claims 1, 2, 4-9, 11, 12, 14-17, 19, 20-22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Mitchell (WO 97/22250).

The limitations of independent claims 1, 8, 11, 16 and 21 are set forth above. Mitchell teaches a nucleic acid molecule comprising a target binding domain of at least 15-30 and up to several hundred nucleotides in length, a safety sequence, a 3' splice region comprising a branchpoint, a pyrimidine tract and a 3' splice acceptor site, a spacer region that separates the 3' splice region from the target binding domain, and a nucleotide sequence to be trans-spliced (see especially the legend for Figure 1 beginning on page 6). Thus Mitchell teaches all of the limitations of independent claims 1, 8, 11, 16 and 21 and dependent claims 4 and 24. Mitchell further teaches the nucleic acid molecule which further comprise sequences encoding a translatable protein product according to the limitations of claims 6, 14 and 19, comprising a sequence encoding a toxin according to the limitations of claims 15 and 20 (see especially Example 1, beginning on page 14) and comprising a translational stop codon according to claim 7 (see especially the second paragraph on page 11).

Independent claim 2 is directed to a cell comprising a nucleic acid molecule wherein the nucleic acid molecule comprises: a) one or more target binding domains wherein said target binding domain is between 10 and 600 nucleotides in length; b) 5' splice site; c) a spacer region that separates the 5' splice region from the target binding domain; and d) nucleotide sequence to be trans-spliced, wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell. Independent claim 9 is directed to a cell comprising a vector wherein the vector expresses a nucleic acid molecule having the limitations of the nucleic acid molecule of claim 2. Independent claim 12 is directed to a method of producing a chimeric RNA molecule in a cell comprising contacting a target pre-mRNA in the cell with a nucleic acid molecule comprising the limitations of the nucleic acid molecule of claim 2.

Independent claim 17 is directed to a nucleic acid molecule comprising each of the limitations of the nucleic acid molecule of clam 2 and further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site. Independent claim 22 is directed to an expression vector which expresses a nucleic acid molecule comprising the limitations of the nucleic acid molecule of claim 2. Mitchell teaches that the nucleic acid molecule described above can include a 5' splice sequence located downstream of the toxin gene, thus separated from the target binding domain (see especially page 11, lines 29-30, and page 12, lines 33-34). The nucleic acid molecule further comprising a 5' splice sequence, and vector and host cell comprising said nucleic acid molecule, taught by Mitchell *et al.* meet the limitations of independent claims 2, 9, 12, 17 and 22. Claim 5, which depends from claim 2 and is limited to comprising a safety nucleotide sequence, is anticipated for the reasons set forth above regarding claim 4. As Mitchell teaches each of the limitations of the claimed invention, the claims are anticipated by Mitchell.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
May 7, 2003

JAMES KETTER
PRIMARY EXAMINER